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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/259,929	03/01/1999	ANTHONY CERAMI	10162-004-99	5875

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EXAMINER	
CHONG, YONG SOO	
ART UNIT	PAPER NUMBER
1617	

MAIL DATE	DELIVERY MODE
02/14/2008	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	09/259,929	CERAMI ET AL.	
	Examiner	Art Unit	
	YONG S. CHONG	1617	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *31 October 2007*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-6,8-14,17-19,48,50 and 58-61* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-6,8-14,17-19,48,50 and 58-61* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☒ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *10/31/07*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Status of the Application

A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on 10/31/2007 has been entered.

Claim(s) 7, 15-16, 20-47, 49, 51-57 have been cancelled. Claim(s) 60-61 have been added. Claim(s) 1-6, 8-14, 17-19, 48, 50, 58-61 are pending. Claim(s) 1 and 48 have been amended. Claim(s) 1-6, 8-14, 17-19, 48, 50, 58-61 are examined herein.

Applicant's arguments have been fully considered but found not persuasive. The rejection(s) of the last Office Action are maintained for reasons of record and modified below as a result of the new claim amendments.

Double Patenting

The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. See *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970);and, *In re Thorington,* 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent is shown to be commonly owned with this application. See 37 CFR 1.130(b).

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

Claims 1-6, 8-14, 17-19, 48, 50, 58-59 are provisionally rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 57-76 of copending Application No. 10/783,052. Although the conflicting claims are not identical, they are not patentably distinct from each other because the claims sufficiently overlap in scope. The latter claims are directed to a method of modulating the immune response in a mammal to an antigen by implanting a device comprising a polymeric material containing the antigen within a second polymeric material, where all of the polymers overlap in scope and the forms of administration are disclosed.

This is a provisional obviousness-type double patenting rejection because the conflicting claims have not in fact been patented.

Response to Arguments

Applicant's request that the double patenting rejection(s) be held in abeyance until allowable subject matter is identified is acknowledged.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which

said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

The factual inquiries set forth in Graham vs John Deere Co., 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

Claims 1-6, 8-10, 12-14, 18-19, 50, 58-61 are rejected under 35 U.S.C. 103(a) as being obvious over Barr et al. (US Patent 5,593,697) in view of Andrianov et al. (US Patent 5,529,777).

The instant claims are directed to a method of modulating the immune response in a mammal to an antigen by implanting a device comprising a polymeric material containing the antigen within a second polymeric material.

Barr et al. teach a pharmaceutical implant comprising a water insoluble material containing an antigen within a polymer coat (abstract) for the prophylactic or therapeutic vaccination (col. 3, lines 16-21) of a mammal (col. 4, lines 32-36). Vaccines against bacterial, viral, fungal, or protozoal infections of animals or humans may be utilized in the device of this invention (col. 6, lines 61-64). Barr et al. disclose that those skilled in the art will be able to recognize the various biocompatible polymers that can be used in this invention (col. 3, lines 52-55). One or more layers of different polymers may be used and when exposed to normal physiological pH conditions, the rupture time of the antigen from the polymer coat is typically between 14 to 45 days (col. 4, lines 9-14).

This bilayer film coating forms an impermeable barrier to the antigen until such time for rupture (col. 5, lines 1-16). The preferred polymers are but not limited to polyethylene, silicone, acrylic resins, and polylactide-glycolide copolymers (col. 5, line 60 to col. 6, line 15).

Barr et al. discloses that those skilled in the art will also appreciate that other biodegradable polymers may be used in this device. The thickness and permeability of the films can be varied by the type of polymer and/or the addition of more than one polymer so as to form a delayed release formulation (col. 5, lines 46-57). Barr et al. also teach that polymers that have holes in the coating thus forming pores which then permit release (col. 6, lines 26-49). It is within the skill of the art to vary the size and number of these pores so as to optimize the release of the active agent. For example, since silicone tubing is well known in the art, it is obvious to perforate a portion of the tubing for the same purpose.

It is noted that the device as disclosed by Barr et al. will intuitively attract cells of the immune system to encounter the antigen and modulate an immune response, because of the fact that a composition and its properties are inseparable. Examiner also notes that once the antigen is introduced into the body of a mammal, it is intuitively bioavailable for inducing or enhancing the immune response (col. 5, line 40).

Applicant has argued that the device that Barr et al. discloses includes an interior and exterior film, which allows fluid to access the core that promotes swelling and subsequent release of the antigen. Thus, a perforated impermeable diffusion barrier would be contrary to the goals of Barr et al. This is found not persuasive since Barr et

al disclose the same material used for the diffusion barrier. Despite the absence of a "diffusion barrier" per say in the disclosure of Barr et al., one is actually present in the device. Furthermore, the release of the antigen is irrelevant because Barr et al. discloses the rupture period to be well after 10 days.

Finally, Barr et al. disclose that the invention is susceptible to variations and modifications other than those specifically described (col. 15, lines 20-23). Thus, it is intuitive to optimize the invention so that the antigen can be repeatedly introduced to the device before or after implantation. Furthermore, it is obvious to one of ordinary skill to optimize the device so that the antigen is immediately bioavailable or in a delay release formulation. Therefore, introduction of the antigen 2-4 days after implantation is within the skill of the art. It is also obvious to optimize the size and number of pores in the polymer coat or tubing.

"When the general conditions of a claim are disclosed in the prior art, it is not inventive to discover the optimal or workable ranges by routine experimentation. *In re Aller*, 220 F.2d 454, 456, 105 USPQ 233, 235 (CCPA 1955); see also *In re Peterson*, 315 F. 3d at 1330, 65 USPQ 2d at 1382 "The normal desire of scientists or artisans to improve upon what is already generally known provides the motivation to determine where in a disclosed set of percentage ranges is the optimum combination of percentages." MPEP 2114.04.

Claims 11, 17, and 48 are rejected under 35 U.S.C. 103(a) as being obvious over Barr et al. (US Patent 5,593,697) as applied to claims 1-6, 8-10, 12-14, 18-19, 50, 58-61 in view of Andrianov et al. (US Patent 5,529,777).

Barr et al. teach as discussed above, however, fail to disclose specifically the removal of the device and the subsequent harvesting of immune cells for the preparation of a hybridoma.

Andrianov et al. teach antigens encapsulated by polymers to form microparticles to induce an immune response in an animal (col. 25, lines 50-57). The preferred biodegradable polymers include polycarbonates, polyesters, polyurethanes, polyamides, polyvinyl alcohol (PVA), gelatin, alginate, polyvinylpyrrolidone (PVP), methyl cellulose (col. 4, lines 1-37), polystyrene, polyvinyl acetate, and copolymers of the polymers or monomers thereof (col. 5, lines 9-21). Andrianov et al. also disclose encapsulating hybridoma cells in the microspheres (example 1). Andrianov et al. also disclose the production of antibodies by oral administration of an influenza vaccine in a polymer to mice as measured by in vitro and in vivo immune response studies (example 4). In the same manner, Example 7 and Table 6 also show harvesting of immune cells (IgC isotopes of the antibodies) in the parental immunization of mice with influenza particles formulated in polymeric microspheres. In this manner, it has been shown that the device containing the immune cells have been removed from the body before the apparent rupture period to begin the harvesting procedure.

It is noted that hydroxylated polyvinyl acetate is obvious over the teaching of polyvinyl acetate since a genus render the species obvious. Examiner notes that this is

a typical genus/species situation. Once a *prima facie* case of obviousness is established, the burden is shifted to the Applicant for objective evidence for nonobviousness. See MPEP 2144.08.

Therefore, it would have been prima facie obvious to a person of ordinary skill in the art, at the time the claimed invention was made, to have removed the device as disclosed by Barr et al. and begin harvesting of immune cells for the preparation of a hybridoma as taught by Andrianov et al.

A person of ordinary skill in the art would have been motivated to have removed the device from the body and begin harvesting of immune cells for the preparation of a hybridoma because: (1) both Barr and Andrianov et al. teach devices comprising antigens encapsulated by polymers to induce an immune response in an animal; and (2) the added advantage of forming a hybridoma for the production of a large amount of a specific antibody. Therefore, one of ordinary skill in the art would have had a reasonable expectation of success in removing a device from the body to harvest immune cells for the formation of hybridoma cells for the production of an antibody in modulating an immune response in a mammal.

Response to Arguments

Applicant argues that the Barr device works in a different manner than the instant invention because Barr et al. does not describe a perforated container, but a impermeable film coating, so that immune cells cannot enter with the antigen.

This is not persuasive because Barr et al. indeed discloses these limitations. First of all, it is noted that the same polymers that are claimed in the instant invention are taught by the cited prior art references. Secondly, Barr et al. clearly teaches the existence of holes or pores in the film coating (col. 6, lines 26-49). Thirdly, Barr et al. teaches the pulse release of antigens even before rupture of the device, therefore an immune response does occur. Premature rupture is not an issue that Barr et al. must deal with since these devices are stable for up to 14-45 days.

Applicant's arguments directed to the limitations addressed in Barr et al. that are not in the Andrianov reference is not persuasive since a reference in an obviousness rejection cannot be attacked individually. Andrianov et al. teach antigens encapsulated by polymers to form microparticles to induce an immune response in an animal. The formation of hybridoma cells is taught as well.

In response to applicant's arguments against the references, one cannot show nonobviousness by attacking references individually where the rejections are based on the combination of references. See *In re Keller*, 642 F. 2d 413, 208 USPQ 871 (CCPA 1981); *In re Merck & Co.*, 800 F. 2d 1091, 231 USPQ 375 (Fed. Cir. 1986).

Conclusion

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Yong S. Chong whose telephone number is (571)-272-8513. The examiner can normally be reached on M-F, 9-6.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, SREENI PADMANABHAN can be reached on (571)-272-0629. The fax phone number for the organization where this application or proceeding is assigned is (571)-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

YSC